REMARKS

Claim amendments

Claims 16, 17 and 19-21 have been canceled without prejudice. Applicants reserve the right to file a continuing application or take such other appropriate action as deemed necessary to protect the subject matter of the canceled claims. Applicants do not hereby abandon or waive any rights in the subject matter of the canceled claims.

Claim 1 has been amended to indicate that "LTR" is the abbreviation for long terminal repeat and that the "promoter is located upstream of the coding sequence and drives expression of the coding sequence." Support for the amendments can be found, for example on page 2, line 23 and page 8, lines 26-28.

Claim 4 has been amended to indicate that the coding sequence is "heterologous to the vector." Support for the amendment can be found, for example, on page 7, lines 24-25.

Claim 5 has been amended to recite a proper Markush claim.

Claim 6 has been amended to delete the term "strong".

Claim 10 has been amended to delete the phrase "the first component". In addition, Claim 10 has been amended to an independent format by incorporating the language of Claim 1, the claim from which it originally depended. Therefore, support for independent Claim 10 can be found, for example, in original Claim 1.

Claim 11 has also been amended to an independent format by incorporating the language of Claim 10, from which it originally depended, and Claim 1. Therefore, support for independent Claim 11 can be found, for example, in original Claims 1 and 10.

Claim 18 has been amended to further clarify the method. In particular, Claim 18 has been amended to recite a method for introducing a nucleotide sequence into target cells comprising contacting the target cells with recombinant retroviral particles according to claim 11, wherein the nucleotide sequence is selected from the group consisting of a nucleotide sequence which is homologous to the target cell, a nucleotide sequence which is heterologous to the target cell and combinations thereof; and maintaining the cells under conditions in which the target cells are infected with the recombinant retroviral particles, thereby introducing the nucleotide sequence into the target cells. Support for the amendment can be found, for example, on page 6, line 26 through page 7, line 9; page 7, lines 24-25; and the Figure.

New Claims 22-24 have been added. Claim 22 has been added to include dependent Claim 3 in an independent format. Therefore, support for Claim 22 can be found, for example, in original Claims 1-3. Support for Claims 23 and 24, which depend from Claim 22, can be found, for example, in original Claims 4 and 5.

Priority

The Examiner acknowledges Applicants' claim for foreign priority based on Application No. 0005/98 filed in Denmark on January 6, 1998, but notes that a certified copy of the application has not been filed.

A certified copy of priority document DK 0005/98 is being filed concurrently herewith.

Objection to Claim 1

The Examiner objects to Claim 1 because of the recitation "LTR" in line 2. The Examiner states that an "abbreviation should be defined upon the first appearance in the claims" (Office Action, page 2).

Claim 1 has been amended to define "LTR" as long terminal repeat, thereby obviating the objection.

Rejection of Claims 19-21 under 35 U.S.C. §101

Claims 19-21 are rejected under 35 U.S.C. §101 "because the claimed recitation of a use, without setting forth any steps in the process, results in an improper definition of a process" (Office Action, page 3).

Claims 19-21 have been canceled without prejudice. Applicants reserve the right to file a continuing application or take such other appropriate action as deemed necessary to protect the subject matter of the canceled claims. Applicants do not hereby abandon or waive any rights in the subject matter of the canceled claims.

Rejection of Claims 19-21 under 35 U.S.C. §112, second paragraph

Claims 19-21 are rejected under 35 U.S.C. §112, second paragraph "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards

as the invention" (Office Action, page 3). The Examiner states that "since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass" (Office Action, pages3-4).

Claims 19-21 have been canceled without prejudice. Applicants reserve the right to file a continuing application or take such other appropriate action as deemed necessary to protect the subject matter of the canceled claims. Applicants do not hereby abandon or waive any rights in the subject matter of the canceled claims.

Rejection of Claims 1-21 under 35 U.S.C. §112, second paragraph

Claims 1-21 are rejected under 35 U.S.C. §112, second paragraph "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention" (Office Action, page 4).

The Examiner states that in Claim 1 "[i]t is unclear exactly which genes the promoter is positioned to drive the expression of" (Office Action, page 4).

Claim 1 has been amended to indicate that the "promoter is located upstream of the coding sequence and drives expression of the coding sequence."

The Examiner states that in Claim 4 "[i]t is unclear what the DNA is heterologous to (vector or cell?) thereby rendering the claim indefinite" (Office Action, page 4).

Claim 4 has been amended to indicate that the DNA is "heterologous to the vector."

The Examiner states that recitation of "and/or" in Claims 5, 10 and 18 "is considered to be improper Markush language because it is unclear what is actually encompassed by the claims thus rendering the claims indefinite" (Office Action, page 4).

Claims 5, 10 and 18 have been amended to delete the phrase "and/or".

The Examiner state that in Claim 6 the "metes and bounds of the term 'strong' are unclear thereby rendering the claim indefinite" (Office Action, page 4).

Claim 6 has been amended to delete the term "strong".

The Examiner states that "Claim 10 is unclear as it does not recite a 'second component' as is implied by the recitation of the 'first component' in line 2" (Office Action, page 4).

Claim 10 has been amended to delete the phrase "the first component".

The Examiner states that in Claim 18 "[i]t is unclear what the nucleotide sequences are homologous and/or heterologous to thereby rendering the claim indefinite" (Office Action, page 5).

Claim 18 has been amended to indicate that the nucleotide sequence is homologous or heterologous to the target cell.

The Examiner states that in Claim 18 "[t]here is no positive process step which clearly relates back to the method recited in the preamble" (Office Action, page 5).

Claim 18 has been amended to recite positive steps which clearly relate back to the method recited in the preamble.

As amended, the claims particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Rejection of Claims 16, 17 and 19-21 under 35 U.S.C. §112, first paragraph

Claims 16, 17 and 19-21 are rejected under 35 U.S.C. §112, first paragraph "as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention" (Office Action, page 5). The Examiner states that the "claims are broad in that they encompass a pharmaceutical composition that can be used in any gene therapy protocol to alleviate any disease and/or condition" (Office Action, page 5). Citing Verma *et al.*, Anderson *et al.*, and Palu *et al.*, the Examiner states that "there is a lack of conclusive evidence that gene therapy protocols are successful in the treatment of human disease" (Office Action, page 7). It is the Examiner's opinion that "[b]ased on the broad scope of the claims, the nature of the invention, the skill of those in the art, the unpredictability of the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue experimentation by one of skill in the art to use the claimed recombinant retroviral vector system in gene therapy protocols for the treatment of human disease" (Office Action, pages 8-9).

Applicants respectfully disagree. Nevertheless, in order to expedite prosecution, Applicants have canceled Claims 16, 17 and 19-21. Applicants reserve the right to file a continuing application or take such other appropriate action as deemed necessary to protect the

subject matter of the canceled claims. Applicants do not hereby abandon or waive any rights in the subject matter of the canceled claims.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTS

Claim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

1. (Amended) A retroviral vector comprising one or more promoters inserted in antisense orientation within the 5' [LTR] long terminal repeat (LTR) region and one or more coding sequences inserted in antisense orientation within the 3' LTR region, both[,] the promoter as well as the coding sequence[,] inserted in such a way as to ensure that the promoter and the coding sequence become duplicated during the process of reverse transcription in a target cell and appear in the 3' as well as in the 5' LTR region of the resulting provirus in a fashion where the promoter is located upstream of the coding sequence [allowing it to drive gene] and drives [gene] expression of the coding sequence.

4. (Amended) The retroviral vector according to claim 1, wherein said coding sequence comprises [heterologous] DNA which is heterologous to the vector.

5. (Amended) The retroviral vector according to claim 4, wherein said coding sequence is selected from one or more elements of the group consisting of marker genes, therapeutic genes, antiviral genes, antitumour genes, cytokine genes [and/or], toxin genes and combinations thereof.

6. (Amended) The retroviral vector according to claim 1, wherein said promoter is a [strong,] constitutive promoter.

10. (Amended) A recombinant retroviral vector system comprising a retroviral vector [according to claim 1] comprising

a) one or more promoters inserted in antisense orientation within the 5' long terminal repeat (LTR) region and one or more coding sequences inserted in antisense

orientation within the 3' LTR region, both the promoter as well as the coding sequence inserted in such a way as to ensure that the promoter and the coding sequence become duplicated during the process of reverse transcription in a target cell and appear in the 3' as well as in the 5' LTR region of the resulting provirus in a fashion where the promoter is located upstream of the coding sequence and drives expression of the coding sequence [as a first component], and

b) a packaging cell line harbouring at least one [retroviral and/or recombinant] retroviral construct coding for proteins required for said retroviral vector to be packaged.

11. (Amended) A retroviral particle produced by transfecting a packaging cell line of a retroviral vector system [according to claim 10 with the retroviral vector according to claim 10] comprising

b) a retroviral vector comprising one or more promoters inserted in antisense orientation within the 5' long terminal repeat (LTR) region and one or more coding sequences inserted in antisense orientation within the 3' LTR region, both the promoter as well as the coding sequence inserted in such a way as to ensure that the promoter and the coding sequence become duplicated during the process of reverse transcription in a target cell and appear in the 3' as well as in the 5' LTR region of the resulting provirus in a fashion where the promoter is located upstream of the coding sequence and drives expression of the coding sequence, and

b) a packaging cell line harbouring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.

18. (Amended) A method for introducing [homologous and/or heterologous] a nucleotide sequence[s] into target cells comprising

a) [infecting] contacting the target cells with recombinant retroviral particles according to claim 11, wherein the nucleotide sequence is selected from the group consisting of a nucleotide sequence which is homologous to the target cell, a nucleotide sequence which is heterologous to the target cell and combinations thereof;

b) maintaining the cells under conditions in which the target cells are infected with the recombinant retroviral particles,

thereby introducing the nucleotide sequence into the target cells.